## Worldwide Scientific Affairs/Clinical Evaluation 2003 Summer Internship

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Literatu	re Review (	of Smoking l	Behavior Art	icles					
Pulbication Title	Authors	Journal Citation	Population Sample Size	Duration of Study	•	Definitions	Statistical Analysis	Results and Conclusion	Rating (1-5)
Consistency of Nicotine Intake in Smokers of Cigarettes with Varying Nicotine Yields	F. Adlkofer, G. Sherer, A. Biber, W.D. Heller, P.N. Lee, and H. Schievelbe	Nicotine Smokign and the Low Tar Programme (1989)	Study 1: 200 male smokers (mean age 26.0 years); Study 2: 51 male and 52 female smokers	24-36	To determine within-person variation of nicotine intake	N/A	Multiple regression techniques based on a mathematica 1 compensation model	Nearly one-third of the smokers take in relatively low amounts of nicotine, which suggests that these subjects do not smoke primarily for nicotine *  Nicotine intake varied widely between smokers, but wasrather constant for each smoker * A major proportion of the smoking population compensates to a considerable extent, probably for nicotine, and thus might benefit from a decrease in the tar/nicotine ratio in eigarettes * There is a statistically significant correlation between serum cotinine and number of eigarettes smoked per day, although it is relatively weak * Smokers in the high and medium cotinine groups tended to have had a longer smoking career and reported inhaling more deeply than those in the low cotinine group * Mean cotinine levels were higher in men than in women * Relatively weak associations of serum cotinine with either eigarette consumption or the nicotine yield of the eigarettes smoked were found * The magnitudes of the compensation indices clearly demonstrate partial compensation * Compensation was more complete for smokers of lower yield eigarettes	4
Puffing Frequency and Nicotiae Intake in Cigarette Smokers	Ashton, H., Watson, D.W., Marsh, R., and Sadlers, J.	British Medical Journal (1970, volume 3, p. 679-681)	36 smokers (15 females and 21 males, 19- 35 years old)	One time	To determine the effect of puffing on nicotine intake and compensation	N/A	t-tests	* Smokers of cigarettes with high-retention filters took more frequent puffs and obtained nearly the same amount of nicotine as smokers of cigarettes with low-retention filters, both while performing the tasks and during the resting period * Smokers of both types of cigarettes took significantly more puffs and obtained more nicotine per unit time during the resting period than during the tasks * It is possible that smokers automatically adjust the nicotine dose obtained from a cigarette to some "optimum" level which may vary with different activities	3
Rahadakin	Battig, K., Buzzi, R., and Nil, R.	macology	STROPOTO (10)	90 minute session	To compare puffing behavior quantitatively across smokers of different types of cigarettes and to estimate inhalation by measure both CO yield of the cigarettes and CO levels in expiratory tidal air	Puffing behavior - number of puffs, puff interval, puff duration, peak pressure, average and total puff volume	Correlational analysis; factor analysis; discriminant analysis; and partial correlation procedures	* Puff shape, puff volume, and puff frequency accounted for about 50% of variation obtained with the different puffing variables * Expiratory tidal CO levels increased with the number of cigarettes smoked before the tests and with the intensity of the smoking habit, but pre- to postsmoking change in tidal CO differences were similar for smokers of all types of cigarettes * Volume compensation for differences of smoke yield fo the cigarettes was generally morep ronounced in women than in men, and, additionally, it was more pronounced for cigarettes with standard smoke nicotine yield below 0.9 mg for both sexes * Only for women, partial correlation procedures suggested that nicotine might be more important in determining puffing behavior than CO and condensate yield, but there were also no women smoking the strongest cigarettes * Personality ratings, pulmonary functions, and cardiovascular functions were not, or only inconsistently, correlated with puffing behavior or type of cigarette	4

C transportage rice	Benowitz,	New England Journal of Medicine (1983, volume 309, p. 139- 142)	272 (122 males, 150 females, average age of 37, all about to begin a smoking treatment program)	One time	To determine whether or not the measured yield of a cigarette corresponds to actual consumption of nicotine (As measured by blood cotinine levels)	N/A	Univariate linear regression and hierarchical multiple linear regression	* Nicotine concentration in tobacco inversely correlated with the concentrations measured by smoking machines * Blood cotinine concentrations correlated with the number of cigarettes smoked per day but not with nicotine yield * Because of long half-life, cotinine concentrations vary relatively throughout a day of smokign and thus are a consistent measure of nicotine exposure * Blood cotinine concentration si not a perfect marker of nciotine consumption, because of individual variability in both the conversion of nicotine to cotinine and the elimination rate of cotinine itself * The main determinants of whether a cigarette has a low or a high yield in machine testing are the charactertistics of its ventilation and burning * These variables are under the control fo the cigarette smoker * Blood cotinine concentration is not a perfect marker of nicotine consumption, because of individual variability in both the conversion fo nicotine to cotinine and the elimination rate of cotinine itself	3
During 1	Benowitz, N.L., and Jacob, P.	Clinical Pharmacol ogy Therapy (1984, volume 35, number 4, p. 499-504)	33.4)	and then again over 2 to 3	To determine the reliability of using certain measures, especially metabolic clearance data, to estimate daily intake of nicotine	N/A	Paired t-test, ANOVA, linear regression	* Translation of blood concentrations into intake is theoretically limited by the fact that metabolic clearance varies considerably from person to person   * The best marker of nicotine intake and exposure was the blood concentration of nicotine measured at 4 PM, followed by the concentration   at noon *  Carboxyhemoglobin concentration at 4 PM and noon were the next best markers * The use of clearance measured ntravenous infusion of nicotine   in the interpretation of blood concentrations of nicotine during smoking   will give a better estimate of nicotine consumption than would   measurement of nicotine exposure during smoking alone * Cigarettes per   day correlate with levels of carboxyhemoglobin or expired carbon   monoxide, plasma or salivary concentrations of thiocyanate, blood levels   of nicotine, and blood or urinary levels of cotinine *  Urinary excretion of cotinine, which is less influenced by urinary flow and   pH, was as good a marker as blood concentrations of nicotine	

Nicotine N	senowitz, on the second	The Journal of Pharmacol ogy and Experiment al Therapeuti cs (1985, volume 234, number 1, p. 153-155)	11 (8 men, 3 women, mean age of 38)	Four 3- dat experime nta! blocks	To determine whether a smoker compensates for accelerated or reduced rate of elimination of nicotine from the body, how complete comepensation is, and how much of the compensation is accomplished by consuming more or less nicotine per cigarette	N/A	Paired t-test	* Average nicotine blood levels were similar in placebo and alkali treatment conditions, but were 15% lower in the acid loading condition * Despite the greater consumption of nicotine in the acid treatment condition, average carbon monoxide level was lower during acid treatment * Carbon monoxide levels were not useful as an indicator of nicotine intake in this study * Urinary acidification increased renal clearance and, to a lesser extent, total clearance and increased daily urinary excretion of nicotine * Daily intake of nicotine was 18% greater during acid loading * The compensatory increase in nicotine consumption was only partial, replacing about half the excess urinary nicotine loss	3
Man P	eyton, J., Fong, I., ad Gupta, S.	The Journal of Pharmacol ogy and Experiment al Therapeuti cs (1994, volume 268, number 1, p. 286-303)	12 smokers (mean age of 34)	13 days	To quantitatively assess human exposure to various metabolites of nicotine; examine the influence of inhalation vs. transdermal administration on the patterns of nicotine metabolism; and assess the extent of recovery of nicotine as various metabolites in people whose systemic intake of nicotine has been measured	N/A	Clearance of metabolites was calculated as dose/area under the concentration time curve (and other metabolic measurement s), paired t or Wilcoxon tests	* A high percentage of a systemic dose of nicotine can be accounted for by measurement of nicotine and its metabolites * The pattern of metabolism is generally similar when nicotine is inhaled or absorbed transdermally * While there is considerable interindividual variability in the pattern of metabolism the pattern is consistent for an individual Within individuals, the extent of conjugation of nicotine and cotinine is highly correlated, but neither is correlated with the extent of conjugation of 3'-hydroxycotinine * Similar enzymes are likely to be involved in the conjugation of nicotine and cotinine and a different enzyme may be involved in the conjugation of 3'-hydroxycotinine	3

the Metabolism Ja and Cardiovascula R.	enowitz, N.L., acob, P., Jones,T., and osenberg, J.	The Journal of Pharmacol ogy and Experiment al Therapeuti cs (1982, volume 221, number 2, p. 368-372)	14 male smokers	30 minutes before infusion, 30 minutes during infusion, and 90 minutes after infusion	To determine individual differences in metabolic and renal clearance of nicotine and the relationship between cardiovascular effects and plasma concentration of nicotine	N/A	Repeated ANOVA with Newman- Keuls post tests, paired t tests, and linear regression	* Infusion of nicotine increased heart rate and blood pressure and decreased fingertip skin temperature in a manner similar to cigarette smoking * Skin temperature declined gradually during nicotine infusion and returned to baseline after infusion in direct relationship to plasma nicotine concentrations * Sensitivity of heart-rate acceleration to low concentrations of nicotine and rapid development of tolerance to higher concentrations suggests that this and perhaps other nicotine-mediated cardiac responses may not differ when smoking low compared to high nicotine cigarettes * The decline in skin temperature, reflecting cutaneous blood flow, was related to blood nicotine concentration Considerable interindividual variability in both metabolic and renal clearance, as well as volume of distribution, were noted * There was no significant correlation between initial concentration of cotinine and metabolic clearance of nicotine	4
Cardiovascula r Effects with Smokeless Tobacco User	enowitz, N. L., Porchet, ., Lewis, S., and acob, P.	Clinical Pharmacol ogy Therapy (1988, volume 44, p. 23-28)	10 male smokers	4 successiv e mornings	To compare the extent and time course of absorption of nicotine and cardiovascular effects of smokeless tobacco with smoking cigarettes and chewing nicotine gum	N/A	Repeated ANOVE with Tukey post hoc tests	* Maximum levels of nicotine were similar but, because of prolonged absorption, overall nicotine exposure was twice as large after single exposures to smokeless tobacco compared with cigarette smoking * All tobacco use increased heart rate and blood pressure, with a tendency toward a greater overall cardiovascular effect despite evidence of development of some tolerance to effects of nicotine with use of smokeless tobacco * Relatively low levels of nicotine and lesser cardiovascular responses were observed with use of nicotine gum	4
with Let of it. Niconiau Nasac Zo	enowitz, N.L., evin, S., nd Jacob, P.	British Journal of Clinical Pharmacol ogy (1997, volume 43, p. 259-267)	12 male smokers (average age of 38)	20 days (4 treatments of 5 days duration each)	To assess sources of individual variability in nicotine and metabolite plasma levels from these dosing systems and from various nicotine sources	N/A	Metabolic elearance analysis, simple and multiple linear regression analysis	* There was considerable individual variation in plasma nicotine and cotinine levels and in the daily dose of nicotine absorbed from various systems, with most variability with nicotine nasal spray and least for transdermal nicotine * Plasma nicotine levels were determined most strongly by nicotine clearance * Cotinine levels were determined most strongly by dose of nicotine and, to a lesser extent, the clearance of cotinine and fractional conversion of nicotine to cotinine * Variability in plasma levels most likely due to wide variability in individual pharmokinetics and in dose delivery from the products	4

Puffing Topography as a Determinant of Smoke Exposure  Bridges, R.B., et al.	Pharmacol ogy, Biochemist ry, and behavior (1990, volume 37, p. 29-39)	170 male smokers (mean age of 37.8)	One time	To determine if differences in puffing topography were associated with cigarette yield and to determine the relationships of puffing topography with population or smoking history characteristics and smoke exposure or blood absorption (i.e., blood concentrations of thiocyanate, carboxyhemogl obin, nicotine or cotinine)	N/A	ANOVA, univariate and multivariate analyses	* Of the puffing topography variables, interpuff interval appeared to be the primary determinant of blood concentrations of smoke constitutents * Smokers of low nicotine yield cigarettes partially compensated for these lower yields by increasing the total volume puffed per cigarette Observed differences in puffing topography associated with increased daily cigarette consumption and cumulative smoking history were consistent with a higher smoke exposure per cigarette * Although both alcohol and coffee consumption are associated with present and cumulative smoking history, coffee consumption is uniquely associated with differences in puffing topography consistent with a higher smoke exposure per cigarette * Neither coffee nor alcohol consumption histories added significantly to the prediction of blood concentrations of smoke constituents over that obtained by smoking history and puffing topography	3
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Assessing Changes in Topography (Inhalation Profile) and Biological Effects of Tobacco Smoke in Humans		N/A.	N/A	To review and give recommendations for analyses of low-ignition cigarettes and toxicity and carcinogenicity	* Toxicity - function of the concentrations of toxic constituents present in smoke and amount of smoke inhaled and retained by smoker * Topography of smoking - inhalation profile of a smoker * Carbon monoxide - gas phase consituent useful as a measure of the depth of inhalation of cigarette smoke (half-life: 4 hr) * Hydrogen cyanide - found in gas phase and metabolized to thiocyanate	N/A	* A number of changes contemplated to reduce the potential of cigarettes (e.g., higher porosity paper, less densely packed tobacco, different tobacco blends) may alter the chemical composition of the smoke, potentially changing its toxicity and carcinogenicity, as well as topography * Any new agent added to the cigarette, and its pryolysis products, have the potential to increase the toxicity of the smoke or to add qualitatively different toxicities * smokers who smoke lower yield cigarettes compensate by changing puff volume and frequency * The short half-life CO in the blood means that the levels are heavily influenced by the intensity of smoking in the hours immediately prior to measurement * Nicotine and cotinine levels are very specific measures of exposure to tobacco smoke, and cotinine levels are the most widely accepted measure of smoking status and the amount of smoke retained is imprecise * recommends a brand-to-brand comparison of risk using machine testing, bioassay testing, a listing of additives used in the cigarette brand, and, finally, human testing	4
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A Further Study of FTC Yield and Nicotine Absorption in Smokers	Byтd, G.D., et al.	Psychophar macology (1998, volume 139, p. 291 299)	72 male smokers	3 days	To determine the relationship between nicotine yield as determined by the FTC method and nicotine absorption	lower FTC yield	Linear regression analysis	* The correlation of the relationship for nicotine absorbed per cigarette was positive and significant but weaker than in previous studies * Only smokers in the highest yield range showed any statistical difference from smokers in the lower ranges * FTC nicotine yield is weakly related to nicotine absorption * Smoker-controlled factors exert a great influence on the amount of nicotine absorbed by smokers * Compensation is substantial but incomplete for the minority of smokers at the low end of the yield scale	3
Importation ogical Factors in Nicoline Self-Administration	Caggiula, A.R., et al		Review of several studies	N/A	To determine the role of nonpharmacolo gical factors on the use of nicotine		N/A	* Direct, pharmacological actions of nicotine are necessary but not sufficient to explain either the high rates of self-administration exhibited by laboratory animals or cigarette smoking by humans * Tolerance to the antiociceptive or coticosterone-elevating effects of nicotine, established by repeatedly injecting nicotine in one environment, was substantially reduced or completely eliminated when an injection of nicotine was given to the same animal in a different environment * The tolerance that develops under normal laboratory conditions is significantly dependent on environmental stimuli that the animal associates with receiving the drug Acquisition of self-administration was also enhanced by combining neutral unconditional stimuli * Nonpharmacological factors may be more important in the drug taking behavior of female humans and rats, and pharmacological factors more important for males * Studies demonstrate that nicotine produces only modest primary reinforcing effects, but potent enhancement of the reinforcing effects of other stimuli	4

	Medical Hypothesis (1985, volume 17, p. 285-297)	Review of several studies	N/A	To explain and support and new hypothesis on puffing intensity and nicotine smoke concentration	requency of	Chi-square	* Changes in puffing intensity during smoking are related not to the control of nicotine uptake but to the modification of cigarette smoke composition * Nicotine reduces the acute airway response to irritant components of cigarette smoke * Smokers may attempt to balance the amount of tar and nicotine in the smoke which they draw from a cigarette in order to facilitate inhalation of irritating smoke * It is the nicotine concentration in the particles of smoke, rather than yield, that is the principal determinant of the amount of smoke inhaled * Smokers, while smoking a single cigarette, will alter their pattern of puffing in response to the increase in tar to nicotine ratio (and hence decline in nicotine concentration) that is known to occur as a cigarette is progressively consumed * When tar yield was controlled for, smokers of cigarettes with higher yields of nicotine puffed larger volumes of smoke from their cigarettes * There appears to be a relationship between the directions of change in cigarette smoke composition and volume-related measures of puffing intensity	3
Pathophysic P., gical Effects of MacLeod, Nicotine on the Pancreas: An, Update Rayford, P.L.	Experiment al Biological Medicine (2002, volume 227, number 7, p. 445-454)	N/A	N/A	To analyze the genetics of nicotine dependence and its role on the development of pancreatic diseases	drug of abuse *	N/A	*Recent CY2PD6 genotyping studies seem to identify an association between efficient metabolizers, lung cancer, and moderate smoking exposure *Experiments show reduced numbers of D2 dopamine receptors in the brains of individuals with AI allele *Subjects with reduced numbers of dopamine receptors may use nicotine to increase brain dopamine levels * Lower production of 5-HTT produces lower levels of serotonin reuptake in individuals, which may produce neurotic effects that leave an individual more at risk for nicotine dependence *Higher activity of COMT or MAO enzymes could lower dopamine levels *Urinary amylase levels higher in smokers *Smoking can result in decreased volume and bicarbonate output by the pancreas, forming duodenal ulcers in humans *Pancreatic enzymes are elevated with either smoking or nicotine * Nicotine induces effects via signal transduction pathways in the pancreatic acinar cell, leading to enhanced levels of intracellular calcium release, resulting in cytotoxicity *Activation and expression of protooncogene, H-ras, can increase cytosolic calcium	4

Cigarette Yields of Tar and Nicotine and Markers of Exposure to Tobacco Smoke	Coultas, D.B., Stidley, C.A., and Samet, J.M.	American Review of Respiratory Discases (1993, volume 148, p. 435- 440)	(39.6% males and 60.4%	One time	To determine the relationships between yields of cigarettes currently smoked and levels of salivary cotinine and end-expired carbon monoxide	N/A	Spearman correlation coefficients and multiple linear regression models	* Spearman correlation coefficients between the current number of cigarettes smoked and cotinine or carbon monoxide were higher than correlations between the Federal Trade commission nicotine data and these same markers * Correlations between FTC tar and carbon monoxide yields and the biologic markers were similarly weak * The current number of cigarettes smoked was the most important predictor of cotinine and carbon monoxide level * Males tended to have higher level of biomarkers and smoked more cigarettes per day than females * Hispanics tended to have lower levels of biomarkers and smoked less cigarettes per day than non-Hispanics	2
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Machine Smoking Results Compared to Human Uptake of Cigarette Smoke	Internation al Journal of Clinical Pharmacol ogy, Therapy, and Toxicology (1987, volume 25, number 3, p. 143-147)		N/A	To review recent studies on plasma concentrations and the application of pharmokinetic parameters in human smoking, specifically looking at the topics of smoking behavior, self-regulation and compensation when switching between different brands, and the relationship between in vitro machine smoking yields and actual human uptake		N/A	* The widely believed opinion that cigarettes with low yields, when in vitro tested, are less hazardous, must be questioned * For the majority of cigarette brands there is no defensible correlation between in vitro analytical machine yields and actual uptake and bioavailability * In one study, 52 percent of smokers admitted to having blocked the ventilation holes of low-yield cigarettes * A second study demonstrated that smokers automatically adjusted the actual nicotine dose of intake to some "optimum value" * In another study, plasma nicotine and COHb concentrations showed that the smokers compensated downward or upward for a switch to high yield or low yield cigarettes, respectively, for about two-thirds of the difference in standard yields when switched to either high or low-nicotine cigarettes * In yet another study, plasma nicotine and cotinine levels demonstrated that subjects' compensation was partial and averaged 36 percent * One study showed that average nicotine intake per cigarette did not correlate with machine-determined yield	5
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AVVCC SSS CONTRACTOR TO SSS	Behavior Therapy (1981, volume 12, p. 507-519) * St smi	· I ami	understand nicotine regulation by studying puff patterns of smokers when they are smoking cigarettes that vary in nicotine yield, or when they have the same cigarette available but serum nicotine y2: levels are lowered during withdrawal or		ANOVA, Pearson product- moment correlation procedures	* There were adjustments in smoking behaviors when cigarettes that vary in nicotine delivery were used, but not when serum nicotine was modified by withdrawal or deprivation * Inhalation patterns of individual cigarettes may not be sensitive to fluctuations in serum nicotine, while they are sensitive to cigarettes that vary in nicotine yield and draw resistance * Subjects take significantly more puffs on the low nicotine cigarette, smoke at a faster rate, hole each puff longer, smoke the cigarette in less time, take more total volume, and more volume/puff * Each subjects showed greater intake of the low nicotine cigarette than the high nicotine cigarette * Both group and individual results suggest that smoking behavior is stable across withdrawal phases * There were no differences in smoking topography in smoking the terminal cigarette after smoking four or no cigarettes during the two hours	5
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What smokers Believe about Light and Ultralight Cigarettes	Etter, J., Kozlowski , L.T., and Perneger, T.V.	Medicine	494 smokers and exsmokers (49% male, average age of 40 years)	One time survey	To assess the knowledge of smokers and exsmokers about light cigarettes and nicotine yields and their perception of the risk of lung cancer, and to identify the characteristics of smokers of light cigarettes	Nicotine and tar numbers printed on cigarette packs represent nicotine or tar yields in smoke under artifical smoking conditions, not the content in cigarettes of nicotine and other compounds	ANOVA, t- tests, Chi- square tests, and multivariate logistic regression model	*Participants estimated that one would have to smoke low light cigarettes or four ultralight cigarettes in order to inhale the same amount of nicotine as that in one regular cigarette * Most participants answered that the risk of lung cancer was the same between light and regular cigarettes, though 27% believed that the risk was lower * Most people believed that the number of milligrams of nicotine printed on the cigarette packs indicated nicotine contents of the cigarettes and not machine-determined yield in smoke * In a multivariate model, smoking mild, light, or ultralight cigarettes was associated with females, a lower Fagerstrom dependence score, an intention to quit smoking, and an intention to decrease cigarette consumption	4
Singularity Topographis and phopin Blood Sevela	Hatsukami , D.K., Pickens, R.W., Svikis, D.S., and Hughes, J.r.	Addictive Behaviors (1988,	10 smokers (five male, five female, average age of 32.3 years)	Seven days	To determine the relationship between smoking topography and nicotine blood levels	N/A	Pearson correlation coefficients	* Change in pre- and post-cigarette nicotine levels and metabolic half-life for nicotine were not related to within-cigarette topography measures or nicotine yield of cigarette, but were significantly related to intercigarette interval * All 10 subjects demonstrated an increase in nicotine blood levels after smoking a cigarette * The greater the change in pre- and post cigarette nicotine blood levels, the longer the intercigarette interval * Subjects with longer half-life for nicotine have longer intercigarette intervals	2

Smokers' Behaviour and Exposure to Cigarette Yield and Smoking Experience	Hee, J., et al.	Pharmacol ogy, Biochemist ry, and Behavior (1995, volume 52, number 1, p. 195-203)	198 (9 groups of 12 subjects, 43 males and 65 females, mean age of 22.7 years)	2 sessions	To determine the influence of cigarette yield and length of smoking experience on smoking behavior and biomarker levels	Steady-state smokers - smokers who have never changed their class of cigarette throughout their smoking life	BMDP statistical software used; ANOVA, multiple regression models	* COHb levels after the first cigarette in the morning increase significantly with CO cigarette yield and length of smoking experience * In the evening, only the cigarette yield has an effect on COHB level * Only COHB level and total urinary nicotine metabolites (Barlow index) are weakly correlated with cigarette yield * The strongest correlation is observed between Barlow index and COHb percentage, whatever the time of the day * The biomarkers, except thioethers and mutagens, are more generally affected by consumption and smoking parameters * Inhalation depth increases with decreasing cigarette yield and with length of smoking habit * Biomarker levels excreted in urine are generally lower for females than for males and tend to increase with smoking history	5
Puff Volume Increases when Low- Nicotine Cigarettes are Smoked	Herning, R.I., Jones, R.T., Nachman, J., and Mines, A.H.	British Medical Journal (1981, volume 283, p. 187- 189)	24 smokers (14 male and 10 female, mean age of 30 years)	3 test days	To determine the effect of nicotine yield of cigarettes on smoking variables	N/A	ANOVA	* Smokers took longer puffs when smoking cigarettes delivering lower nicotine yields than their normal brands * The number of puffs and interval between puffs did not differ between nicotine doses * Subjects took more time to smoke high-nicotine cigarettes * Increase in heart rate was greater with high- and medium-nicotine levels than with low * Increase in breath CO concentrations after subjects had smoked was consistent with the increase in puff volume with these cigarettes * Mean volume of puffs decreased with each puff * Smokers, although they increased puff size, were either unable or unwilling to inhale enough smoke to compensate completely for the reduced nicotine yield	5
How A Cigardia Supplied Determine Blood Misotri	Herning, R.I., Jones, R.T., Benowitz, N.L., and Mines, A.h.	Clinical Pharmacol ogical Therapeuti cs (1983, volume 33, number 1, p. 84-90)	11 smokers (8 males and 3 females)	One session on one day or one session on each of two days	topography and machine-	* Puff volume- the volume of smoke passing through a cigarette holder * Interpuff itnerval - the time from the start of one puff to the start of the next * Inhaled volume - the amount of air and smoke inhaled at the maximum inspiration	Univariate linear regression analysis and multiple regression analysis (as well as log- linear regressions)	* Indirect evidence suggests that smoking low-tar and nicotine cigarettes does not necessarily reduce exposure to these substances * Machine-determined nicotine yields of the cigarettes correlated with the increase in nicotine blood levels after smoking but, when individual differences in smoking behavior were taken into account along with the nicotine yield, there was a stronger correlation with nicotine blood levels	3

W +4.56	Nil, R., d Battig, K.	Pharmacol ogy, Biochemist ry, and Behavior (1991, volume 40, p. 139-149)	72 males and 72 females	2 sessions	assess the stability of	* Upregulation - intensifying smoking of "lighter"	ANOVA, posteriori Scheffe- tests, Pearson correlations	*For plasma nictoine, higher nicotine yield cigarettes produced higher presmoking levels * For plasma cotinine, higher nicotine yield cigarettes produced higher presmoking levels * There was no difference in respiratory CO for higher nicotine yield cigarettes * Pre- to postsmoking boosts of CO and nicotine increased with yield, but the differences were smalelr than those in yield * This partial compensation can be attributed to puffig behavior as revealed by the differences between yield classes with respoect to flowmeter measures (puff volume, flow parameters, number of puffs) * Contact condition (whether smoking with lip contact or with a flowmeter holder) hardly influenced results * Forced puffing revealed down regulation mechanisms in smoke absorption and, less pronounced, in puffing behavior * Cardiovascular and subjective effects were widely independent of yield * Plasma cotinine appeared as the best smoke exposure indicator, due both to its high retest relaibility and its relationship to nicotine yield	
Regulation and C	ozlowski , L.T., Jarvik, I.E., and ritz, E.R.	Clinical Pharmacol ogy and Therapeuti cs (1974, volume 17, number 1, p. 93-97)	56 undergradua tes (32 males and 24 females)	One time	To determien whether there is nicotine regulation in cigarette smoking	N/A	Planned comparison F tests	* High nicotine cigarette preloads were followed by longer latencies to the next cigarette than were the low nicotine cigarette preloads * High nicotine gum preloads were followed by less puffing on the subsequent cigarettes than were the low nicotine gum preloads * Subjects did light up sooner after a low nicotine cigarette than after a high nicotine cigarette - thus a nicotine regulation effect did occur	3

Cigarette Filter Ventilation is a Defective Design because of Misleading Taste, Bigger Puffs, and Blacked Vents	Kozlowski , L.T., and O'Conner, R.J.	Tobacco Control (2002, volume 11, p. i40-i50)	Approximat ely 250 documents	N/A	To review tobacco industry documents on filter ventilation in light of published studies and to explore the role of filter ventilation in the design of cigarettes that deliver higher smoke yields to smokers than would be expected from standard machine smoked tests	Compensation - the attainment of higher smoke exposures by human smokers of lower tar cigarettes than by standard smoking machines	N/A	* Filter ventilation misleadingly makes cigarettes taste lighter and milder and, therefore, they appear less dangerous to smokers * Filter ventilation promotes compensation mainly by facilitating the taking of larger puffs For very heavily ventilated cigarettes, behavioral blocking of vents with lips or fingers is an additional contributor to compensatory smoking Published smoker exposure studies have seen little difference in biomarkers of exposure among smokers of Light, Ultra Light, and lowest tar brands * Recent reviews of the disease effects of lower standard tar cigarettes find little support for actual risk reduction as a result of the use of such cigarettes	4
Misuse of "Light" si Cigarette for Means of Van Biocking	, L.T., Pillitteri, J.L., and Sweeney,	Journal of Substance Abuse (1994, volume 6, p. 333-336)	158 discarded light cigarette butts	Collected over 5 months	To determine the rate of vent hole blocking in light cigarettes	N/A	N/A	Extreme vent blocking was found in 27&, some vent blocking in 26%, and no vent blocking in 47% of butts	3
Estimating provided in Supplement of Tar Sylventing and Cartion Municipal from the Lowest Hillard Filter-Cigarettes	Kozlowski , L.T., et al.	British Journal of Addiction (1982, volume 77, p. 159-165)	46 low- yield smokers (7 males and 39 females, average age of 34)	One time	To evaluate the behavioral misuse of low- yield, ventilated filter cigarettes	N/A	N/A	* 52% of low-yield smokers admitted to having blocked the ventilation holes on these cigarettes at some time with either lips (20%), fingers (39%), or tape (20%) * Although only three smokers admitted blocking the holes at the present time, 41 percent gave evidence of currently blocking the holes * In comparison to standard assays, modified smoking machines with vent holes blocked show a tar increase of 15- to 39-fold nicotine increase of 8- to 19-fold, and CO increase of 10- to 43-fold * 94% ° of participants said they smoke low-yield cigarettes because they thought them to be safer, milder, less likely to produce physical symptoms, and the first step to quitting *  Participants who gave evidence of being very effective hole-blockers reported that they took less time to have their first cigarette of the day than subjects who gave no indication of being hole blockers	5

Is Nicotine Important in Tobacco Smoking?  Kumar, R., Cooke, E.C., Lader, M.H., and Russell, M.A.H.	Clinical Pharmacol ogy and Therapeuti cs (1976, volume 21, number 5, p. 520-529)	12 smokers (seven males and 5 females)	3 sessions	To determien whether nicotine intake is the basis for the tobaccosmoking habit	N/A	Multivariate analyses and ANOVA	* Subjects differed considerably between themselves in their rates of puffing, but individual rates tended to remain broadly stable during the test session * Inhaled doses reduced the volumes subsequently puffed in an orderly manner * Roughly similar doses of nicotine, given intravenously, completely failed to alter subsequent smoking as measured by volumes puffed * Inhaled doses systematically reduced the speed to the first puff; intravenous nicotine did not * Heart rate was systematically altered by doses of the drug * Beta EEG activity was increased with increase in nicotine (both smoking and intravenously) * The lack of effect of intravenous nicotine on smoking cannot be ascribed either to inadequate dosage or to a failure of the drug to enter the blood and the brain	
Nicother ded Smoking Lader, M. Belavior	British Journal of Clinical Pharmacol ogy (1978, volume 5, p. 289-292)	N/A	N/A	To review studies on nicotine's effect on smoking behavior	*Nicotine -at higher doses depresses the activity of cholinoceptors in autonomic ganglia and nueromuscular junction; releases catecholamines; depresses spinal reflexes, excites respiration through stimulation of carotid body, activates electroencephalogia; increases slowwave electroencephalographic activity, decreases alpha activity, increases beta activity; increases heart rate, blood pressure, muscle blood flow, skin blood flow inhibition, and adrenaline excretion	N/A	*Smoking improves performance in the low-arousal test in the low-arousal smokers (those who smoke to alter themselves or to combat boredom) but slightly impaired it in the high-arousal smokers (those who smoke to calm themselves) and vice-versa for high-arousal tasks ttes under low-arousal condition, but nitoctine intake altered *Withdrawal and tolerance effects are seen, but whether they are related solely to nicotine is unknown *There is a decrease in the number of cigarettes smoked, time smoked, and puff frequency with an increase in nicotine yield * It is impossible for the average smoker to increase his smoking sufficiently to compensate fully for the low content of low-nicotine cigarettes * The number of cigarettes per day of smokers is unaffected by tar content * Smokers detected differences in the surength of cigarettes based on nicotine and not tar content * Nicotine gums have varied effects on smoking behavior * Forced intake of nicotine by injection not as strong as should be * Cotinine and urinary pH measurements good indicators	4

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Modeling Smoking History: A Comparison of Different Approaches	Leffondre, K., Abrahamo wicz, M., Siemiatyck i, J., and Rachet, B.	Journal of Epedimiolo gy (2002,	640 primary lung caases, 430 population controls, and 485 cancer controls	1979- 1985	To elucidate the impact of several decisions that must be made when modeling smoking variables	* Smoking status - never/current/exs moker * Smoking intensity - number of cigarettes or packs smoked per day	Adaptation of Cox's model	* The estimated hazard ratios for current and ex-smokers depend strongly on how long subjects are required to not have smoked to be considered "ex-smokers" * When the aim is to estimate the effect of continuous smoking variables, it may be preferable to discount some recent exposure and use a cutoff of approximately two years for defining ex-smokers * Using intensity and duration as separate variables may lead to a beter model fit than using their product (cigarette-years) * The effect of intensity was significantly stronger among current smokers than among ex-smokers, whereas the effect of duration was significantly lower * Among current smokers, using cigarette-years underestimates the impact of intensity and overestimates the impact of duration * When estimating the effects of time since cessation or age at initiation, it is still useful to use cigarette-years, because it reduces multicollinearity * Of 40 articles published in 2000, there was considerable variation in both the nature of the data collected on smoking history and the way the data were used in analyses	5
Relationships of Contentified Human Smoking Behavior and Demographic Variables	Moody, P.M.	Soc. Sci. Med. (volume 14, p. 49- 54)	517 smokers (mean age of 39.1)	Survey	To determine the relationship between aspects of smoking behavior and sex, race, age, education, income and socioeconomic status	N/A	Product- moment correlations	* Patients from lower socioeconomic groupings had a greater number of puffs, shorter intervals between puffs, larger puff duration, shorter cigarette butts, and more daily tar and nicotine intake than the subjects from upper socioeconomic groupings * Males and older patients had longer puff duration, greater puff volume and more daily tar and nicotine intake than their counterparts * Relatively large standard deviation on all parameters of smoking behavior suggests much variability in "how" and "how much" people smoke * The characteristics of the cigarettes smoke were very different in various countries * Income and education levels were negative associated with number of puffs per cigarette * Whites had longer puff duration than nonwhites and had higher levels of tar and nicotine intake * The average puff duration of 2.12 seconds was significantly higher than reported in previous studies	

Inhalation: Is B	Nil, R., Buzzi, R., nd Battig, K.	Pharmacol ogy, Biochemist ry, and Behavior (1986, volume 24, issue 3, p. 587-595)	117 regular smokers (69 male, 48 female)	To determine the effect of cigarette yields on topography measures, smoking behavior, and smoking absorption	N/A	Multiple regression analysis, cross- sectional correlations, t-tests	* Pre- to postsmoking CO boost remained unrelated to the smoke deliveries of the cigarettes in both comparisons (interindividual and switching) * Estimated mouth intake of nicotine was strongly dependent on the smoke yield variables of the cigarette but remained uncorrelated with CO absorption * Discrepancies between mouth smoke intake and alveolar smoke absorption could not be explained by the volumes or durations of the postpuff respiratory cycle * Females had a lower blood pressure and smoked lighter cigarettes than men * There was an increases in puff volume with the lighter cigarettes * There was some compensation for differing nicotine yields, mainly among puffing variables * There were some sex differences in how cigarette yield affected smoking behavior	3
Patterneon W Smollers. Vinti P	Nil, R., Woodson, P.P., and Battig, K.	Clinical Science (1986, volume 71,	19 (13 female and 6 male) high CO absorbing smokers and 20 (12 female and 8 male) low CO absorbing smokers	To determine whether differences in CO absorption between two groups might be paralleled by differences in personality dimension scores, by differences in the coronary prone type A behaviour pattern or by particular life style and consummatory behaviors	* High CO absorbers - CO boosts greater than 3.5 ppm * Low CO absorbers - CO boosts less than 1 ppm	N/A	* High CO absorbers differed from low CO absorbers by more intensive patterns of puffing and respiratory inhalation, by higher daily cigarette and coffee consumption, by lower alcohol consumption, by shorter latencies to the first cigarette in the morning, by greater subjective need for smoking and by lower scores for healthy eating habits * No intergroup differences were observed for smoking induced heart rate acceleration * The high CO absorbers were significantly older than the low CO absorbers; however, no evidence was found that any of the differences in smoking style between the two extremes might be related to their difference in age * No differences were seen in cigarette strengths, in personality or in coronary prone behaviour as assessed by means of standardized questionnaires in all subjects * Nicotine plays a more important role in smoking motivation among the high than among the low CO absorbing smokers	3

Individual Differences in Nicotine Intake per Cigarette	Paterson, F., et al.	Cancer Epidemiolo gy, Biomarkers , and Prevention (2003, volume 12, p. 468-471)	seeking smokers (95 males and 95 females, median age of 45.9	One time (two smokes, 40 minutes apart)	To investigate the demographic, smoking status, and psychological predictors of nicotine boost; specifically to determine whether negative affect would be associated with higher levels of nicotine boost (presumably to attenuate negative mood symptoms) and whether African Americans and males would have higher nicotine boost levels than Caucasians and women	individualized measure of how much nicotine has been extracted from smoking a	ANOVA, t- tests, Pearson correlations, and lincar regressions models	*Positive affect (mood) was a significant positive predictor of nicotine boost, controlling for baseline cotinine levels and cigarette brand nicotine delivery *Peek seekers may be seeking more positive reinforcement from smoking, such as modulation of arousal *Race was a significant predictor of boost for the comparison of African-American with Caucasian participants *Age was marginally associated with nicotine boost, but gender, education, and body mass index were not *Smoking rate and cotinine level were marginally associated with boost, whereas nicotine/cotinine ratio, menthol/nonmenthol brand, cigarette type, and nicotine dependence were not *Negative affect and depression symptoms were not related to nicotine boost	4
Service that Physiologic Effects for Menthal and Normal That Cigar ettes with Diffecting Nicoting Delivery	Pickworth, W.B., Moolchan, E.T., Verlin, I., and Murty, R.	ogy, Biochemist ry, and Behavior	18 menthol and 18 nonmenthol cigarette smokers (mean age of 32.6 years)	3 cigarettes smoked 45 minutes apart	To determine the influence of menthol and nicotine yield on the sensory and physiologic effects of smoke delivered nicotine	N/A	Repeated measures ANOVA, Greenhouse- Geisser epsilo adjustment, Bonferroni's method	* Commercial and high-yield cigarettes increased heart rate and blood pressure more than low-yield cigarettes; although, no differences in exhaled carbon monoxide occurred * Participants smoked average yield commercial cigarettes faster and with fewer puffs than either of the research cigarettes (high and low yield) indicating production difference can affect topography * High-yield nonmenthol cigarettes reduced craving and were rated as more satisfying than high-yield menthol cigarettes * No differences between menthol and nonmenthol cigarettes on other subjective measures (strength, physiological reward, negative effects) were observed * Nicotine delivery, but not mentholation, influences cardiovascular and most subjective measures	4

Examining the Relation between Usual Brand Nicotine Yield Blood Cotinine Concentration, and the Nicotine-"Compensation" Hypothesis	Pritchard, W.S., and Robinson, J.H.	Psychophar macology (1996, volume 124, p. 282 284)	Eight data sets	N/A	To determine whether or not the nicotine- "compensation" hypothesis holds true based on a review of eight studies examining the effect of nicotine yield on blood cotinine levels	Nicotine- "compensation" hypothesis - all smokers achieve a specific level of nicotine in their blood, regardless of the FTC nicotine yield of the cigarette smoked	Linear regression analysis	* There is wide variability in blood concentrations over the range of FTC nicotine yields * The nicotine-compensation hypothesis is not supported * On average, blood cotinine concentrations are found to be roughly midway between complete compensation and the value expected if there was no compensation * As a result of individual smoking behavior differences the data indicate that on average, smokers achieve roughly 50% lower blood cotinine concentrations than predicted by the nicotine compensation hypothesis * Long-term switching to a lower-yield brand involves a transient phase where compensation is high followed by a steady-state phase where compensation is lower * Studies indicate that switching to a lower-yield cigarette for several weeks does result in a significant drop in blood cotinine concentration - may be even more profound in voluntary switchers * Data indicate that on average a smoker switching from a 1.0 mg product to a 0.5 mg product would, after several weeks of adjustment, achieve a 25% reduction in nicotine intake	4
A Comparative Study of the Amount of the Sounce Low Vield Low Vield Cless Cigarettes	Robinson, J.C., Young, J.C., and Rickert, W.S.	British Journal of Addiction (1982, volume 77, p. 383-397)	22 smokers	8 weeks	To determine levels of non-invasive exposure measures with low yield cigarettes to identify compensation effects	N/A	Two interaction cotnrasts and ANOVA	*The non-invasive exposure measures employed (average number of cigarettes per day, daily mouth level nicotine intake, butt length, expired air carbon monoxide and saliva thiocyanate) demonstrated that the almost complete compensation of the treatment group was achieved with a combination of increased cigarette consumption, smoking intensity, and depth of inhalation * Compensation occurred through increase in cigarette consumption, increase in puff intensity, and hole blocking Expired air carbon monoxide and saliva thiocyanate levels remained the same during all three periods	3
Mercamylande ne Incress Nicotine Preferenties Action duses Nicotine Discriptions	Rose, J.E., Sampson, A., Levin, E.D., and Henningfie Id, J.E.	Pharmacol ogy, Biochemist ry, and Behavior (1989, volume 32, number 4, p. 933-938)	8 male smokers	Five sessions	To determine the effect of mecamylamine on nicotine preference (discrimination, intake, enjoyment, and desire)	Mecamylamine - a nicotinic receptor blocker	ANOVA	* When the subjects evaluated puffs of smoke with high and low nicotine content, mecamylamine caused a dose-related decrease in the self-rated strength and harshness of the high nicotine dose level smoke * In contrast, there was little effect of mecamylamine on the low dose smoke * At the highest mecamylamine dose (20 mg) there was no significant difference in the ratings of high and low nicotine eigarettes * Low doses of mecamylamine decreased the reported desire for a cigarette, and also attenuated the reduction in desire for a cigarette caused by smoking * When the subjects were allowed to select their preferred level of nicotine intake using a smoke mixing device, the 10 and 20 mg doses of mecamylamine caused a significant increase in self-administered nicotine level * Despite this compensatory increase in nicotine self-administration, the reduction in desire for a cigarette after smoking was still less than after placebo	4

Relationship between Cigarette Yields, Puffing Patterns, and Sinoke Intake: S.R., e Evidence for Tar Compensation ?	' I (1982	55 smokers	One time (during afternoon or evening)	To examine the relationship between cigarette yields, puffing patterns, and blood nicotine and COHb concentrations in a sample of smokers smoking their usual brand of cigarette	N/A	Regression analysis	* Total volume of smoke puffed from a cigarette was a more important determinant of peak blood nicotine connentration than the nicotine or tar yield of the cigarette, its length, or the reported nubmer of cigarettes smoked on the test day * When nicotine yield was controlled for, smokers of lower-tar cigarettes not only puffed more smoke from their cigarettes than smokers of higher-tar cigarettes but they also had higher plasma nicotine concentrations, suggesting that they were compesnating for the reduced delivery of tar by puffing and inhaling a greater volume of smoke * The results based on carboxyhemoglobin concentrations were consistent with this interpretation * CO yield was the onyl variable to have a significiant effect on carboxyhemoglobin levels * Subjects who had not smoked for more than half an hour tended to puff more intensely * Older people puffed less than younger people and women puffed more than men	5
Effective Pull Number and Pull Special Weinhold Weinhold Exposure from Contest of Exposure from	d Rehavior	6 smokers (mean age of 36.3)	27 smoking trials for first experime nt, 9 trials for second experime nt (3 trials per day)	To further clarify how smoking behaviors (puff number and puff spacing) can influence biological exposure to CO from commercial brand cigarettes	N/A	ANOVAs, Tukey's post- hoc tests	*CO exposure (pre- to postsmoking increments) was directly related to the number f puffs taken for all cigarette yields *CO exposure from the highand low-yield cigarettes was equivalent when the number of puffs taken from the low-yield cigarettes was increased by 50% *In contrast, CO exposure from ultralow-yield cigarettes was still marginally lower than exposure from high-yield cigarettes after a 4-fold increase in puff number *Puff spacing did not affect biological exposure to CO *The number of puffs taken during smoking can clearly affect biological exposure to CO, but compensation for lowered yield using increased puffs is much more difficult when ultralow- as compared with low or "light"-yield cigarettes are smoked	4

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One Study 1: 6 t	To better understand nicotine regulation by studying udy 1: puff patterns of smokers	were adjustments in smoking behaviors when cigarettes that vary in nicotine delivery were used,	Subjects were asked to monitor nd report urges to smoke, where and with whom a cigarette			nia-, <u>n</u>	
smokers in estal base reduction program (3 males and 3 females, mean age 31.8 years)  * Study 2: 7 solbkers (2 males and 5 females, mean age of 13.5 females are selected by the selected base of 13.5 females are selected base on the selected base of 13.5 females are selected base on the selected base on the selected base on the selected base of the selected base on the selected base of the select	ablish when they are smoking cigarettes that vary in nicotine dat 2- yield, or when they week ervals fter cigarette available but serum nicotine levels are lowered during	but not when serum nicotine was modified by withdrawal or deprivation * Inhalation patterns of individual cigarettes may not be sensitive to fluctuations in serum nicotine, while they	was smoked, and their general mood * Pressure I ansducer used to measure umber of ouffs per cigarette, ength of time smoking the cigarette assessed	ANOVA, Pearson product moment correlation procedures			
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8 (9 groups 12 subjects, males and 5 females, can alre of 2.7 years)	levels after number the first cigarette in the morning increase significantly with CO cigarette yield and length of smoking experience arette and the of king cinence oking vior and total with COHB level and total with cigarette els nicotine metabolites (Barlow correlated with oby cigarette yield * The strongest try in extraorder less number of the strongest try in extraorder less number of the first part	ff  ff  ff  ff  ff  statistical software used; and ANOVA, multiple regression models  d  d  d  d  d  d  d  d  d  d  d  d  d	* The absence of significant differences due to cigarette class in urinary biomarkers can be explained by changes in inhalation depth, individual differences of metabolism, and limited specificity of some markers					
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	* Indirect evidence suggests	* Puff volume was the	, , , ,		 	 4-11-11-11-11-11-11-11-11-11-11-11-11-11	
One or session on to one day or males and 3 one 1 females) session on deach of two days	that smoking low-tar and nicotine cigarettes does not necessarily	volume of smoke passing through a cigarette holder * Pressure transducer attached to holder to measure interpuff interval, number of puffs, and puff duration * Depth of inhalation was measured by mercury capillary strain gauges * Expired-	Univariate linear regression analysis and multiple regression analysis (as well as log-linear regressions)	Persons smoking more or less often than the smokers tested might show different relationship; other subsets of smoking measures might give an even better relationship			
	along with	was					

24 smokers (14 male and 12 female, mean 3 test days age of 34 years)	* Smokers took longer puffs when smoking cigarettes delivering lower nicotine yields than their norma brands * The number of puffs and interval between puffs did not differ between puffs did not differ between nicotine doses * Subjects took more time to smoke high nicotine cigarettes *	rate was recorded continuou sly * CO values obtained before and 30 minutes after with an Ecolyzer (Series 2000) * A checklist of mood and tobacco symptoms completed before and after smoking * Puff	ANOVA	Subjects did not like the cigarettes because they were unfiltered, had no flavoring agents, and were dry; the highnicotine cigarettes made subjects feel light-headed and shaky; CO concentration is found to be a good indicator of chronic plasma nicotine concentration but was not an indicator of			
	cigarettes on smoking variables  Subjects took more time to smoke high nicotine	tobacco symptoms completed before and after smoking * Puff volume and duration, number of puffs, and interpuff interval were		concentration is found to be a good indicator of chronic plasma nicotine concentration			

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20 smokers (half menthol smokers, thean age 37,4 years)	d cigarette produced significant greater boost in C *   Mentholat d cigarette decreased average and total cumulativ regular cigarettes on select chemical and topographi c parameters and according to race to the smoke or inhalation of the	demograp y hics and current smoking habits give * Fagerstro m d Tolerance scale and Control Dependen ce scalc given * Questionn aire about from the smoking given * Spiromete tresting was given test * The cigarette holder trestind	Subject averages taken; inhaled volume adjusted to get foreed vital capacity; 3-way ANOVAs performed			
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measures of smoke was higher postpuff in the dark tobacco category postpuff
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117 regular Smokers (69 minute session female)	To determine the effect of cigarette yields on topography measures, smoking behavior, and smoking absorption t	* Pre- to postsmokin g CO boost remained unrelated to the smoke deliveries of the cigarettes in both comparisons (interindivid ual and switching) * Estimated mouth intake of nicotine was strongly dependent on the smoke yield variables of the cigarette but remained mcorrelated with CO absorption  * Discrepanci es between mouth smoke intake and	with a pressure transducer and digital analyzer were used to determine puff volume, puff duration, puff interval, peak pressure, latency to peak pressure, and peak	SPSS and BMDP software was used; cross- sectional correlations; comparisons of means by t-test	Subjects recognized low yield cigarettes immediately and rated them as less satisfactory		
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To examinate and compare the smoking two products 21 of cigarettes with 20 minute products breaks in between products were of different tar yield.	numbers were marginally higher in the 6 mg group than in the other two * All 3 group exhibited a similar downward tend on puff volume and duration  regarette during puff process measured by attaching cigarette to a exhibited a holder incorporat ing an tend on puff volume and duration with two	Smokers unfamiliar with a product of lower delivery may smoke in a more intense manner for other sensory reasons		
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To exami	volume of kept a record of puffed from their a cigarette was a more important determinant determinant ne of peak volume sample separate volume.				
cigarette yields, puffing One time patterns (during and bloom stemments for afternoon nicotine	n cocnentratio and collected nicotine or tar yield of their butts * A d cigarette, its length, or the reported nubmer of cigarettes smoked on the test day puffs taken, the yield was pressure	Regression Analysis			

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1	ľ	retention	was							i e
		filters took	recorded							
		more	by an							ŀ
		frequent	observer							
	1	puffs and	and time							
		obtained	of start							
	1	nearly the					-			
	l	same	of each				ļ			
		amount of								
		nicotine as				1				
	_	smokers of								
	То	cigarettes	Cigarette							
	determine	with low-	stubs							
36 smokers (15	the effect	retention	were			•				
females and 21 One time	of puffing	filters both		t-tests						
males, 19-351	on nicotine	while	for	t teats						
years old); j	intake and	performing	nicotine				]			
	compensati	the tasks	content							
	on	and during	(nicotine							
1 K K K		the resting					•			
<b>计划: 门槽</b>		period *	to		!					
		Smokers of								
		both types	*							
		of cigarettes	1							
		took	y rate was							
		significantly								
		more puffs					ĺ			
		and	by impodens							
		and obtained	impedanc			ĺ				
			e						İ	
		more	pneumogr						[	
		nicotine per								
Auri ing saniti) persita		unit time	means of				L	 		

			* Puff	* A	-		r		 
			shape, puff	cigarette					
			volume, and	holder-					
		!	puff	puffing					-
			frequency	flow					
			accounted	meter was		Ì			
			for about	used to				į	
		To	50% of	determine			]		
		compare	variation	puffing				,	
	I	pufting	obtained	flow and					
		behavior	with the	pressure					1
		quantitativ	different	* Module			•		1
		ely across		developed		1			
		smokers of		to analyze					
	ı	different	Expiratory	puff	Correlational				ĺ
67 mala and 42		types of	tidal CO	volume,	analysis; factor				i
67 male and 43 female 90	minute	cigarettes	levels	puff	analysis; discriminant	Intersex differences in			
	ession	and to	increased	duration.					
years old)	casion	estimate	with the	peak	analysis; and partial	puffing behavior			
75.13	i	inhalation	number of	pressure,	correlation				
		by measure		latency to	procedures			<b>.</b>	
	1	both CO	smoked	peak	procedures				
		yield of the	before the	pressure,					
		cigarettes	tests and	and					]
	ŀ	and CO	with the	interval					
		levels in	intensity of	from the					
				preceding					
		tidal air	habit, but	puff *					
	Ī			Expirator					1
	1		postsmokin						
	1	ļ	g change in			ļ			1
			tidal CO	and					ŀ
	- 1		differences	analyzed			•		
			were similar	with					
Harris Constitution			for smokers	Ambient					

272 (122 males, 150 temales, 150 cip con 37, all about to begin a smoking freatment programs me	* Nicotine concentration in tobacco inversely correlated with the concentrations measured by smoking machines * Blood cotinine concentrations measured by high performant ce liquid chromato graphy * Blood samples were taken and measured for nicotine yield * Because of long half-life, cotinine concentrations with nicotine yield * Because of long half-life, cotinine concentrations with gas chromato graphy  * Nicotine concentrations measured by high performant ce liquid chromato graphy * Blood samples were taken and measured for nicotine intake with gas chromato graphy  * Nicotine concentrations measured by high performant ce liquid chromato graphy * Blood samples were taken and measured for nicotine intake with gas chromato graphy	Univariate linear regression and hierarchical multiple linear regression						
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in puffing volume topography and associated duration
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			* When	* Brooth			 1	<del></del>	
				* Breath					
		1	using the	co					
			Accord, the	sample					
				was taken					
,			of smoking-	*					
			induced	Fagerstro					
			craving	m				İ	
		l	reductions	nicotine					
		[	and the	tolerance					
1		l	physiologic	questionn					
			al effects of						
		l	smoking	*VAS			į	·	
		То	were less,	subject-		Subjects were			
1		determine	and puff	rated		only mildly			
10 light or		the effects				dependent;			
ultra-light		of Accord	frequency	on	ANOVA; Hunh	received only			
	m	on.		withdraw	Feldt	acute exposure			
cigarette	Two 2-	subjective	were greater		corrections;	to the novel			
smokers (mean	hour	and	than when	al	Tukey's	system; were not			
ago of 1.1.4	sessions	physiologic		symptoms	significantly	blind to smoking			
years. 7 teats to		al measures	smoked	*	different test	condition; no			
and 3 roule)		and	meirown	Questionn		placebo			
		smoking	brand of	aire of		condition; small			
		behavior	cigarettes *	Smoking		sample size			
		OCHAVIOL	The expired	Urges		Sample Size			
照着新			air CO	(intention					
		l	increases	to smoke					
			after	and					
150			smoking	anticipati					
			own brand	on of					
			cigarettes	relief					
			did not	from					
			occur after	withdraw					
			using the	al) *				I	
				,					
			Accord * The Accord	Heart					
	<del></del>	L	THE ACCORA	raie ckiii.	······································	I			

16 female and 16 male smokers of Four 2.5 light or ultra- light cigarettes (mean age of 25.9 years)	and tachycardia produced by Accord are all less than that produced by normally marketed cigarette brands, even controlling for the system's 8- puff limitation and for brand proferance	at start * Nicotine dependen cy measured by Fagerstro m nicotine- tolerance questionn aire * Quit ANOV attempts history taken * VAS scale to measure tobacco	As; Feld ons; 's inthy it test  of only smokers of light and ultra- light eigarettes limited; subjects were not familiar with Accord system; no control for	
16 female and 16 male smokers of light or ultra- light cigarettes (mean age of 25.9 mars)	the effect of the Accord igarette on withdrawal of suppressio n and biomarkers f exposure  Crgarette brands, even controlling for the system's 8- puff limitation and for brand preference * Incomplete withdrawal suppression	aire * Mixe Quit ANOV attempts history taken * Tuke VAS signific scale to measure tobacco withdraw al	d As; Feld ons; 's limited; subjects were not familiar with Accord system; no	